Information Disclosure Statement.

Applicants note that the Paper Nos. 7 and 9 (signed PTO Form-1449s) were to be enclosed with the Office communication Paper No. 17; however, Applicants did not receive the cited attachments. Applicants respectfully request copies of Paper Nos. 7 and 9 for our files.

Furthermore, Applicants submit herewith a supplemental Information Disclosure Statement and accompanying PTO Form 1449. Applications respectfully request that the cited information be expressly considered during the prosecution of this application, and the reference be made of record therein and appear among the "references cited" on any patent to issue therefrom.

35 U.S.C. §112, First Paragraph.

Claims 1, 6-19, 45, 46 and 58-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification such as to reasonably convey that the inventors had possession of the claimed invention at the time of filing. Applicants traverse.

The Office alleges (paragraph 10) that "in order to satisfy the written description requirement in terms of polynucleotide variants, a recitation of a representative number of polynucleotide variants must be disclosed in the specification, or the genus must be described in terms of the required chemical and structural features that would preserve the function of species within the genus..." and alleges that the written description requirement has not been met due to lack of additional disclosed species. This is in direct opposition to the Guidelines provided by the PTO governing the practice for addressing whether a functional description of genetic material meets the written description requirement. Applicants note that "[t]he written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics which provide evidence that Applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics (66 Fed. Reg. at page 1106).

The claims are drawn to nucleic acids which hybridize under defined stringent conditions (0.02M salt and 60°C) to a member of a specified list of sequences/complement sequences (SEQ ID Nos. 2-10). Applicants have provided structural as well as functional characteristics in the description of the present invention, thereby disclosing "relevant identifying

characteristics which provide evidence that Applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Since the written description requirement has been satisfied according to the guidelines provided by the USPTO, Applicants respectfully submit that the rejection is improper and request that it be withdrawn.

35 U.S.C. §103(a) Rejections

The claims were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of various accession numbers (representing expressed sequence tags, or ESTs) in view of Matthews and Kricka (Analytical Biochemistry 169:1-25, 1988). Applicants traverse.

Claim 1 is drawn toward an isolated nucleic acid molecule comprising a polynucleotide sequence that hybridizes under stringent conditions (0.02 molar salt concentration and a temperature of at least 60°C) to a specified sequence (SEQ. ID. No. 2-10) or to a complement of the specified sequence.

The Office states that "it would have been *prima facia* obvious to one of ordinary skill in the art at the time the invention was made to label the polynucleotide sequences taught by the Accession Number[s] by the methods taught in Matthew and Kricka for use as probes in the further characterization of the polynucleotide sequences of the Accession Numbers, such as restriction mapping of the Accession Number polynucleotide or the detection of mRNA transcripts expressing said of the Accession Number polynucleotide sequences. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Matthews and Kricka."

One requirement for proving a *prima facie* case of obviousness under 35 USC §103(a) is a motivation to modify a cited reference or combine cited teachings to produce the claimed invention (M.P.E.P. § 2143.01). The Office has not established a motivation to combine the cited EST sequence accession numbers with the Matthews and Kricka publication. Specifically, no motivation, beyond a foreknowledge gained by review of the present specification regarding the utility of such sequences, has been provided by the Office. The teaching or suggestion to combine the cited publications must both be found in the prior art and *not based on Applicant's disclosure* (M.P.E.P. § 2143). The cited accession numbers do not provide an indication of their utility, or any

reason for labeling (or motivation to use) the cited compositions for any purpose whatsoever. The Matthews and Kricka publication is alleged to teach various methods for labeling polynucleotide sequences, but do not provide a motivation to label the specific sequences represented by the cited accession numbers.

Applicants also note that, according to the Utility Examination Guidelines (66 Fed. Reg. 1092-1099), "[i]f a patent application discloses only a nucleic acid molecular structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable (p1093). As such, ESTs without an indication of utility would not be considered patentable. The Office cannot on the one hand assert that ESTs are not patentable because they have no utility, and on the other hand state that it would have been *prima facia* obvious to one of ordinary skill in the art to make and use these sequences (e.g. to label them by the methods taught in Matthew and Kricka for use as probes, etc.). The rejection is clearly contrary to stated Office policy with respect to EST sequences.

Since the motivation is not provided by the cited art and cannot be drawn in hindsight from the Applicant's disclosure, and since no other motivation has been provided, Applicants submit that the rejection is improper and respectfully request that it be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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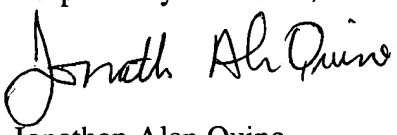
Respectfully submitted,



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Appendix B
copy from 08/731,499 specification

other antibody fragments). While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such Fab' fragments may be synthesized *de novo* either chemically or by utilizing recombinant DNA methodology. Thus, the term antibody, as used herein also includes antibody fragments either produced by the modification of whole antibodies or synthesized *de novo* using recombinant DNA methodologies.

The phrase "specifically binds to a protein" or "specifically immunoreactive with", when referring to an antibody refers to a binding reaction which is determinative of the presence of the protein in the presence of a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein and do not bind in a significant amount to other proteins present in the sample. Specific binding to a protein under such conditions may require an antibody that is selected for its specificity for a particular protein. For example, antibodies can be raised to the a 20q13 amplicon protein that bind the 20q13 amplicon protein and not to any other proteins present in a biological sample. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays are routinely used to select monoclonal antibodies specifically immunoreactive with a protein. See Harlow and Lane (1988) *Antibodies, A Laboratory Manual,* Cold Spring Harbor Publications, New York, for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1(A) shows disease-free survival of 129 breast cancer patients according to the level of 20q13 amplification. Patients with tumors having high level 20q13 amplification have a shorter disease-free survival ($p=0.04$ by Mantel-Cox test) compared to those having no or low level amplification.

Figure 1(B) ~~Shows~~ Shows the same disease-free survival difference of Figure 4(A) in the sub-group of 79 axillary node-negative patients ($p=0.0022$ by Mantel-Cox test).

Figure 2 shows a comparison of 20q13 amplification detected by FISH in a primary breast carcinoma and its metastasis from a 29-year patient. A low level amplification of 20q13 (20q13 compared to 20p reference probe) was found in the primary